parameters accordingly and any quality assurance checks that are deemed necessary. Therefore the adaptive radiation therapy requires more resources when compare to the conventional image-guided radiation therapy. In fact, image-guidance can be considered the first step in adaptive practice as it triggers the initial decision to adapt and provide the 3D volumetric images that are necessary for adaptive re-plan. There have been efforts to create techniques and technologies that can facilitate the adaptive planning. In this presentation, we will first discuss the state of art practice of adaptive proton therapy including the experience at our institution. We will review studies assessing the magnitude of intra- and inter-fractional changes and its impact on delivered proton dose distribution with and without adaptive practice. Secondly, we will present the cutting edge ideas and techniques that are developed specifically for adaptive proton lung therapy in the most recent literature.

[1] Liu HH, Balter P, Tutt T, et al. Assessing respiration-induced tumor motion and internal target volume using 4DCT for radiation therapy of lung cancer. Int J Radiat Oncol Biol Phys 2007;68:531-540
[2] Sonke JJ, Belderbos J. Adaptive Radiotherapy for lung cancer. Semin Radiat Oncol 2010 Apr; 20(2):94-106.

SP-0502

In-vivo range estimation and adaptive particle therapy

T. Lomax[1]
[1]*Paul Scherrer Institute PSI, Centre for Proton Therapy, Villingen, Switzerland*

The finite range of protons is a two-edged sword. On one side, it is the *raison d'etre* of proton therapy, on the other, a potential source of uncertainties in-vivo. As such, both in-vivo range estimates and adaptive therapy are being proposed and pursued for mitigating such uncertainties. However, sources of in-vivo range uncertainties are many, ranging from systematic uncertainties in the calibration of CT Hounsfield units to proton stopping power and inaccuracies in dose calculations (for convenience defined here as type I uncertainties) to variations in patient positioning and anatomy changes during the course of treatment (type 2). Whereas, for good quality CT data, type 1 uncertainties can result in range uncertainties of a few percent or millimeters (about 3% or 6mm in the worst case,) type 2 can result in range changes of the order of centimeters. In addition, type 1 uncertainties will, to a good approximation, be similar across all patients of a particular indication and will remain the same throughout the duration of a patient's treatment. Type 2 on the other hand will be patient and (potentially) treatment day dependent. So, what are the roles of in-vivo range measurement and adaptive therapy for dealing with these? It seems to this author that in-vivo range verification perhaps has a role to play in reducing type 1 uncertainties, whereas the best approach to type 2 has to be adaptive therapy. Adaptive therapy (based on regular, if not daily, imaging) must be pro-active (i.e. the treatment should ideally be adapted *before* delivery), whereas in-vivo range verification can only be (at best) reactive (e.g. may be able to provide a reason to interrupt a delivery if an error is detected). As such, the best use of in-vivo range estimation seems to be as part of a population based (commissioning) approach in order to verify that CT calibration and dose calculations are more and more precise, such that type 1 uncertainties resulting from pre-treatment imaging (necessary to mitigate type 2 errors) can then be reduced as much as possible. Such an approach however puts stringent demands on the accuracy and precision of in-vivo range estimates, with in-vivo resolutions in the millimeter range being required in order to significantly improve these uncertainties. Will this ever be achievable?

SP-0503

European strategy

M. Baumann[1,2,3,4]
[1]*OncoRay – National Center for Radiation Research in Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus- Technische Universität Dresden, Dresden, Germany*
[2]*German Cancer Consortium - DKTK Dresden, and German Cancer Research Center - DKFZ, Heidelberg, Germany*
[3]*Helmholtz-Zentrum Dresden - Rossendorf, Institute of Radiooncology, Dresden, Germany*
[4]*Department of Radiation Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus- Technische Universität Dresden, Dresden, Germany*

One of the most exciting areas of basic, translational and clinical research in radiation oncology today is radiotherapy with particles, i.e. with protons or heavier ions. The main advantage of radiotherapy with protons compared to state-of-the-art radiotherapy with photons is a decrease of the volume of normal tissues irradiated to intermediate and low doses, while irradiation of normal tissues to high doses or the conformality of the dose to the tumor are usually similar for protons and photons. Exceptions include situations where critical normal tissues can be excluded by proton therapy from the irradiated volume completely or to a large extent. The most relevant clinical research question is therefore to investigate whether sparing of normal tissue by proton therapy leads to clinical relevant benefits which balance the higher costs of this treatment. After demonstration of relevant sparing of normal tissues, further clinical studies on utilizing dose intensification strategies may become another important research avenue in those tumors where local or locoregional tumor control today are unsatisfactory.
At present only few centers (often with different technologies and patient populations) are active in clinical research using protons, which makes fresh thinking on study design in radiation oncology necessary, as large scale randomized trials will not be feasible in many situations. Model-based approaches are a major component of the trial methodological portfolio, but alternatives (including multicenter stepwise randomized trials, pseudo-randomized trials and prospective matched pair trials) may be superior in different clinical situations. All of these approaches necessitate dedicated clinical research infrastructures and complex high-level network formation to reach the power for meaningful clinical trials. This also plays an important role in terms of radiotherapy stratified by biological parameters, which is anticipated to become a clinical reality in the near future for several tumor entities.
Proton (or other particle) therapy holds particular promise to further advance personalized radiation oncology. However obstacles in trial design, data sampling and integration, or analysis may dilute the effects to such an extent that it may not be possible to demonstrate it according to generally accepted scientific standards. This would be a major hurdle for further implementation and reimbursement of this auspicious technology, and also for sound medical stratification of access of patients in need for this therapy.
The lecture will discuss opportunities and problems of proton therapy in the context of high precision personalized as well as biologically stratified radiation oncology, thereby also touching trial design, technology development and the importance of network formation on a European level.

Symposium: Small animal irradiation

SP-0504

Preclinical radiotherapy technology, dosimetry and treatment planning

K. Butterworth[1], M. Ghita[1], C.K. McGarry[2], S. Jain[3], G.G. Hanna[3], J.M. O'Sullivan[3], A.R. Hounsell[2], K.M. Prise[1]
[1]*Centre for Cancer Research & Cell Biology Queen's Uni, School of Medicine- Dentistry and Biomedical Sciences, Belfast, United Kingdom*
[2]*Northern Ireland Cancer Centre, Radiotherapy Physics, Belfast, United Kingdom*
[3]*Northern Ireland Cancer Centre, Clinical Oncology, Belfast, United Kingdom*

Small animal image guided irradiation platforms are revolutionizing the field of preclinical radiobiology by facilitating the delivery of clinically relevant irradiation